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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/625,436	ANDERSEN, MARK R.	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 18-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 18-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/31/05; 6/25/04; 9/5/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With regard to Claim 11, the term "Zbig valve" renders the claim indefinite because no clear definition as to what encompasses a "Zbig valve" can be found in the art at the time of invention. An appropriate search of the prior art cannot be performed without a more descriptive definition.

Appropriate clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1, 2, 6, 7, 9, 14-16, 18-26, 33, 34, 36, 38, and 42 are rejected under 35 U.S.C. 102(e) as being anticipated by Stern (U.S. 6,670,153 B2).

With regard to Claim 1, Stern discloses a microfluidic device (Figures 1,2, 5; Columns 8,9, for example) comprising: a first chamber adapted to retain one or more first components for a desired reaction (Figure 2, Section 110; Column 9, Lines 30-40, for example); a second chamber (Figure 2, Section 140; Column 9, Lines 30-40, for example); at least one second component retained in the second chamber, the at least one second component comprising one or more of an enzyme, a catalyst, an initiator, a promoter, and a cofactor, for the desired reaction (Figure 2, Section 140; Column 9, Lines 30-40, e.g. DNA polymerase, for example); and an openable communication between the first and second chambers (Figure 2, Section 190; Column 9, Lines 30-40, for example).

With regard to Claim 2, Stern discloses PCR reaction components in the first chamber (Column 9, Lines 30-40, 55-67, for example).

With regard to Claim 6, Stern discloses an initiator (Column 9, Lines 30-40, e.g. DNA polymerase, for example).

With regard to Claim 7, Stern discloses a promoter (Column 9, Lines 30-40, e.g. DNA polymerase, for example).

With regard to Claim 9, Stern discloses PCR reaction components in the first chamber (Column 9, Lines 30-40, 55-67, for example).

With regard to Claim 14, Stern discloses a third chamber; and an openable communication between the third chamber and at least one of the first and second chambers (Figure 2, Section 190; Column 9, Lines 30-40, for example).

With regard to Claim 15, Stern teaches a method (Column 8, Lines 45-67, for example) comprising: providing a microfluidic device comprising: a first chamber; at least one first component retained in the first chamber, the at least one first component comprising one or more reactant or reagent or component for the desired reaction (Figure 2, Section 110; Column 9, Lines 30-40, for example); and a second chamber; at least one second component retained in the second chamber, the at least one second component comprising one or more of a catalyst, an initiator, a promoter, and a cofactor for a desired reaction (Figure 2, Section 140; Column 9, Lines 30-40, e.g. DNA polymerase, for example); and an openable communication between the first and second chambers; opening the openable fluid communication between the first and second chambers; at least one of combining and mixing the at least one first component with the at least one second component (Figure 2, Section 190; Column 9, Lines 30-40, for example).

With regard to Claim 16, Stern teaches the step of heating the microfluidic device (Column 10, for example).

With regard to Claim 18, Stern teaches double-stranded DNA (Column 8, Lines 15-25, for example).

With regard to Claim 19, Stern teaches denaturation of double-stranded DNA (Column 8, Lines 25-35, for example).

With regard to Claim 20, Stern teaches annealing of single-stranded DNA fragments (Column 8, Lines 25-35, for example).

With regard to Claim 21, Stern teaches nucleic acid amplification (Column 8, Lines 25-35, for example).

With regard to Claim 22, Stern teaches injecting a sample into the first chamber (Column 7, Lines 50-60).

With regard to Claims 23 and 24, Stern teaches chambers pre-filled with nucleic acid amplification reaction components (Column 9, Lines 5-15, for example).

With regard to Claims 25 and 26, Stern teaches chambers pre-filled with nucleic acid amplification sequence detection components (Column 9, Lines 5-15, for example).

With regard to Claim 33, Stern discloses an initiator (Column 9, Lines 30-40, e.g. DNA polymerase, for example).

With regard to Claim 34, Stern discloses a promoter (Column 9, Lines 30-40, e.g. DNA polymerase, for example).

With regard to Claim 36, Stern discloses an enzyme (Column 9, Lines 30-40, e.g. DNA polymerase, for example).

With regard to Claim 38, Stern teaches pre-heating the chambers (Column 10, for example).

With regard to Claim 42, Stern teaches combining, heating, and mixing components (Columns 7,8, for example).

With regard to Claims 43 and 44, Stern teaches heating the reaction components for the purposes of PCR (Column 10, for example), thus, the reaction components are inherently activated and mixed in a thermal manner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 3-5, 8, 30, 32, 35, 37, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stern (U.S. 6,670,153 B2) in view of Bloch et al. (U.S. 5,411,876).

With regard to Claims 3-5, 8, 30, 32, 35, 37, and 40, the disclosure of Stern has been outlined in the above rejections. Stern does not expressly disclose segregating magnesium from other PCR reagents when performing a "hot start" PCR reaction.

Bloch et al. expressly teach the segregation of magnesium from other PCR reagents when performing a "hot start" PCR reaction (Column 4, Lines 1-30, for example). Bloch further teaches several advantages to the segregation of inorganic magnesium such as the fact that segregated magnesium salts prepared "hot start" PCR need not be prepared with special precautions against microbial contamination, a

common problem with mixtures containing enzymes (Column 4, Lines 15-25, for example).

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art to modify the teachings of Stern to perform a "hot start" PCR reaction with segregated magnesium salts since Bloch suggests such a procedure to minimize the need for the incorporation microbial precautions within reaction mixtures.

2. Claims 10, 12, 13, 27-29, 31, 45, 47, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stern (U.S. 6,670,153 B2) in view of Mian et al. (U.S. 6,319,469 B1).

Mian et al. expressly disclose a microfluidic device (Figure 1; Column 6, for example) comprising a variety of systems including microchannels, reagent reservoirs, reaction chambers, etc. (Column 7, for example). Mian further highlights that the invention is advantageously used for microanalysis in biological research applications such as the polymerase chain reaction (Column 35; Column 45, Example 4, for example).

With regard to Claim 10, Mian expressly discloses valves between reaction chambers (Column 7, Lines 35-55, for example).

With regard to Claim 12, Mian expressly discloses valves comprising an adhesive material (Column 19, for example).

With regard to Claim 13, Mian expressly discloses recloseable valves (Column 17, for example).

With regard to Claims 27 and 28, Mian expressly discloses nucleic acid sequence restriction components (Column 46, Example 5, for example).

With regard to Claim 29, Mian expressly discloses combination by centripetal force (Column 17, Lines 15-20, for example).

With regard to Claim 31, Mian expressly discloses ddNTPs (Columns 48, 49, Example 7, for example).

With regard to Claims 45 and 47, Mian expressly discloses mixing by vortexing and shaking (Column 17, Lines 5-35, for example).

With regard to Claim 48, Mian et al. expressly disclose a microfluidic device (Figure 1; Column 6, for example) comprising a variety of systems including microchannels, reagent reservoirs, reaction chambers, etc. (Column 7, for example). Mian expressly discloses valves between reaction chambers (Column 7, Lines 35-55, for example).

The disclosure of Stern has been outlined in the above rejections. Stern clearly demonstrates the use of a microfluidic system with separate reaction chambers to perform a "hot start" PCR with segregated reaction compositions (Figures 1,2, 5; Columns 8,9, for example).

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art to perform a "hot start" PCR reaction in the microfluidic system of Mian since Stern expressly suggests such a reaction within a microfluidic device. A practitioner of

ordinary skill in the art clearly would have been motivated to use the microfluidic device of Mian since they suggest that the invention is advantageously used for microanalysis in biological research applications such as the polymerase chain reaction.

3. Claims 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stern (U.S. 6,670,153 B2) in view of Anderson et al. (U.S. 6,168,948 B1).

The disclosure of Stern has been outlined in the above rejections. Stern does not expressly disclose the drying of reaction components in reaction chambers.

With regard to Claim 39, Anderson et al. disclose a microfluidic device (Columns 17,18, for example) capable of the polymerase chain reaction (Columns 7-10, for example). Anderson further teaches dried (i.e. lyophilized) reaction components predisposed within reaction chambers to provide for maximum shelf life of the overall device (Column 10, Lines 30-55, for example).

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art to perform a "hot start" PCR in the microfluidic device of Stern with lyophilized predisposed PCR reaction components, such as magnesium, since Anderson suggests such a modification for the purpose of increasing the shelf life of the device.

4. Claims 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stern (U.S. 6,670,153 B2) in view of Pomp et al. ("Organic solvents as facilitators of polymerase chain reaction" Biotechniques. 1991 Jan;10(1):58-9).

The disclosure of Stern has been outlined in the above rejections. Stern does not expressly disclose the incorporation of glycerol into the PCR reaction components.

With regard to Claim 41, Pomp et al. disclose that the addition of glycerol to a PCR enhances the reaction (Figure 1, for example).

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art to perform a "hot start" PCR in the microfluidic device of Stern with the incorporation of glycerol into the PCR reaction components, such as magnesium, since Pomp suggests such a modification for the enhancement of the reaction.

5. Claims 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stern (U.S. 6,670,153 B2) in view of Laughharn, Jr. et al. (U.S. 6,948,843 B2).

The disclosure of Stern has been outlined in the above rejections. Stern does not expressly disclose mixing by sonication.

With regard to Claim 41, Laugharn, Jr. et al. teach mixing fluids within microfluidic devices (Columns 1,2, for example) through sonication (Column 9, for example) for the ability to provide gentle local mixing (Column 47, for example).

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art to perform a "hot start" PCR in the microfluidic device of Stern with the incorporation of sonication to mix the reaction components since Laugharn suggest such a modification for the ability to provide gentle local mixing of fluids within microfluidic devices.

Conclusion

Claims 1-16 and 18-49 are rejected. No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Barnes et al. (U.S. 6,403,341 B1).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

3/14/06

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